Memory outcome after temporal lobe epilepsy surgery: corticoamygdalohippocampectomy versus selective amygdalohippocampectomy

Clinical article

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Object. The aim of this study was to compare IQ and memory outcomes at the 1-year follow-up in patients with medically refractory mesial temporal lobe epilepsy (MTLE) due to hippocampal sclerosis. All patients were treated using a corticoamygdalohippocampectomy (CAH) or a selective amygdalohippocampectomy (SeIAH).

Methods. The data of 256 patients who underwent surgery for MTLE were retrospectively evaluated. One hundred twenty-three patients underwent a CAH (63 [right side] and 60 [left side]), and 133 underwent an SelAH (61 [right side] and 72 [left side]). A comprehensive neuropsychological test battery was assessed before and 1 year after surgery, and the results were compared between the surgical procedures. Furthermore, seizure outcome was compared using the Engel classification scheme.

Results. At 1-year follow-up, there was no statistically significant difference between the surgical approaches with respect to seizure outcome. Overall, IQ scores showed improvement, but verbal IQ decreased after left SelAH. Verbal memory impairment was seen after left-sided resections especially in cases of SelAH, and nonverbal memory decreased after right-sided resection, especially for CAH. Left-sided resections produced some improvement in nonverbal memory. Older age at surgery, longer duration of seizures, greater seizure frequency before surgery, and poor seizure control after surgery were associated with poorer memory.

Conclusions. Both CAH and SelAH can lead to several cognitive impairments depending on the side of the surgery. The authors suggest that the optimal type of surgical approach should be decided on a case-by-case basis. (*DOI: 10.3171/2009.10.JNS09677*)

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M ESIAL temporal lobe epilepsy due to HS is the most common form of epilepsy syndrome, and surgical treatment has been shown to be the most effective method of treatment.⁶¹ Surgical success can be mainly attributed to recent developments in diagnostic and treatment modalities that have enabled us to select appropriate surgical candidates who will most likely have favorable seizure outcome with decreased

complications and improved quality of life.^{54,56,58-61} Traditionally, seizure outcome has been used as the only criterion to evaluate the results of surgical treatment and the patient's well-being. However, it has recently been realized that seizure frequency alone after surgery is not sufficient to judge whether a patient is in a favorable condition.

Falconer's standard-type en bloc anterior temporal lobe resection, or CAH,⁸ is still the most commonly used surgical procedure in temporal lobe epilepsy, although there recently has been a trend to perform SelAH³⁶ in an attempt to remove smaller portions of healthy tissue. Despite different surgical modalities, there is still no common consensus as to which approach is better with respect to seizure outcome, neuropsychological impact, and quality of life.^{2,3,5,32,44,49} Therefore, neither SelAH nor CAH can be recommended over the other as a standard

Abbreviations used in this paper: CAH = corticoamygdalohippocampectomy; EEG = electroencephalography; FIQ = full IQ; HS = hippocampal sclerosis; LM = logical memory; MNI = Montreal Neurological Institute; MTLE = mesial temporal lobe epilepsy; PIQ = performance IQ; RAVLT = Rey Auditory Verbal Learning Test; ROCF = Rey-Osterrieth Complex Figure; SeIAH = selective amygdalohippocampectomy; VIQ = verbal IQ; WMS-R = Wechsler Memory Scale-Revised; WAIS-R = Wechsler Adult Intelligence Scale-Revised.

approach. Apart from seizure freedom, cognitive function (the main subject of this paper) is one of the most important criteria for a successful epilepsy surgery. Since Scoville and Milner's initial observation,⁵⁰ there has been no consensus regarding the optimal type of resection in MTLE with respect to cognitive functions, and the findings are less congruent. In 1982, Wieser and Yaşargil⁶² reported on a rather small number of patients and found that SelAH produces less cognitive impairment than CAH. However, their findings were disputed when other studies produced different results a decade later. The more recent studies revealed that side and type of surgery affected cognitive functions, and different results were reported. Some found that SelAH, like CAH, can cause cognitive decline but to a lesser extent,12,16,55 but others did not find differences between the surgical approaches.^{17,26} Furthermore, in a randomized prospective study comparing 2 selective surgical approaches, Lutz et al.³¹ suggested that the transsylvian and transcortical approaches result in significant impairment of verbal memory after left-sided surgery; however, they found that phonemic fluency is improved after a transcortical SelAH but not after the transsylvian approach. Collateral damage after transsylvian SelAH has recently been discussed as a possible source of postoperative memory impairment.²¹

In an attempt to decrease surgical effects on cognitive functioning, subtemporal SelAH has recently been developed for MTLE.^{22–24,53} In subtemporal SelAH, it has been suggested that preservation of the lateral temporal neocortex or temporal stem could explain improvement or preservation of postoperative cognitive functioning.^{23,24,53} Nevertheless, selective resections appear to show better neuropsychological outcome, although this is not a consistent finding. In this report, we selected patients in whom unilateral MTLE was diagnosed and confirmed by imaging and electrophysiological studies, who underwent either CAH or SelAH. Both surgeries were performed by the same surgeon (A.O.) at MNI. The comparison of memory outcome at 1-year follow-up of these 2 surgical techniques is the subject of this report.

Methods

Patient Population

A list of all patients who underwent SelAH or CAH between 1986 and 1999 was obtained from the epilepsy surgery database. The patients who were included in our previously published studies^{55,56} are not included in this study. For this study the inclusion criteria were as follows: patients who 1) were at least 16 years old; 2) had complete clinical, neuroradiological, electrophysiological, and surgical data; 3) had interictal and ictal scalp/sphenoidal and intracranial depth electrode EEG studies displaying unilateral independent anteromesial temporal epileptic discharges; 4) had MR imaging or histopathological findings characteristic of HS; 5) had left hemisphere language dominance revealed by an intracarotid sodium Amytal test (Wada test, or in recent years etomidate speech and memory (eSAM) test] or functional neuroimaging studies; 6) had the same neuropsychological tests pre- and postoperatively; and 7) had a follow-up duration of at least 1 year. In all, 256 patients were seen at regular follow-up examinations by the referring neurologist and the surgeon. Data used for this analysis included the following clinical and demographic parameters: 1) sex; 2) handedness; 3) age at seizure onset; 4) age at surgery; 5) duration of epilepsy; and 6) seizure frequency per month.

First Cohort: Patients With CAH

The first group included 123 patients who had undergone CAH between 1986 and 1990. This group consisted of 64 male and 59 female patients with a mean age of 25.7 \pm 8.0 years. The mean age at seizure onset was 9.3 \pm 8.1 years; 63 patients underwent surgery on the right and 60 on the left side.

Second Cohort: Patients With SelAH

The second group consisted of 133 patients who had undergone SelAH between 1991 and 1999. This group consisted of 59 male and 74 female patients with a mean age of 34.5 ± 10.8 years. The mean age at seizure onset was 10.6 ± 9.2 years; 61 patients underwent surgery on the right and 72 on the left side.

Preoperative Evaluation

The preoperative evaluation included clinical, electrophysiological, and imaging examinations as well as neuropsychological testing. All patients underwent preoperative MR imaging assessments with a 1.5-T (in some cases 3-T) unit (Philips Gyroscan, Philips Medical Systems) including high-resolution T1- and T2-weighted and FLAIR studies. Electrophysiological evaluations included scalp and sphenoidal interictal and ictal EEGs. Prolonged video-EEG with scalp/sphenoidal electrodes was performed to record interictal and ictal spikes during wakefulness and sleep in all patients. Intracranial stereo-EEG recording with stereotactically implanted electrodes was performed when needed in cases in which the extracranial EEG recordings did not provide clear localization or lateralization of seizure onset. Furthermore, if needed, intraoperative electrocorticography recording was used to examine whether there was epileptic activity coming from the neocortex.

Neuropsychological Test Battery

The results of a comprehensive and well-established neuropsychological test battery were reviewed during the preoperative and at the 1-year follow-up periods. Intellectual function was assessed using the WAIS-R, which provides FIQ, VIQ, and PIQ. Verbal learning and memory were evaluated using the WMS-R and the RAVLT. The subtests of WMS-R included "immediate" and "delayed" recall of LM tests. In RAVLT, there are 5 trials of learning and recall of a concrete 15 words, free recall immediately, and delayed recall after 30 minutes followed by word recognition. Learning performance was assessed by summing the total number of correctly reproduced words over the 5 learning trials. Nonverbal or visuospatial (figural) memory was assessed using simple geometric drawing with "immediate" and "delayed" recall and ROCF tests.

TABLE 1: Demographic characteristics in patients with MTLE*

	No. of Patients				
		Rt Herr	nisphere	Lt Hem	nisphere
Factor	Total (256)	CAH (63)	SelAH (61)	CAH (60)	SelAH (72)
mean age (yrs)†	30.3 ± 10.5	36.4 ± 9.2	35.7 ± 11.8	24.9 ± 6.6	33.6 ± 9.9
sex (M/F)	123/133	29/34	28/33	35/25	31/41
handedness (rt/lt)	206/50	46/17	48/13	50/10	62/10
mean age at onset (yrs)	9.9 ± 8.7	11.4 ± 8.3	11.6 ± 9.1	7.1 ± 7.3	9.7 ± 3.1
mean seizure duration (yrs)	20.6 ± 10.7	16.3 ± 8.5	24.0 ± 13.3	17.7 ± 6.9	23.9 ± 10.9
mean seizure frequency/mo	37.6 ± 57.2	40.5 ± 60.3	29.2 ± 46.7	47.8 ± 63.3	33.6 ± 56.9

* Unless indicated otherwise. Mean values are presented as the mean ± SD.

† Mean age at the time of surgery.

Surgical Procedures

Between 1986 and 1990 (when the first group underwent surgery), CAH was considered the standard procedure at MNI for treatment of MTLE/HS. In CAH, the goal is to perform a temporal neocortical resection, extending 5 cm along the sylvian fissure and 5-5.5 cm along the floor of the middle fossa on the nondominant side and 4.5-5 cm on the dominant side. In addition, total or partial resection of the amygdala and uncus is performed, and 2.5-3 cm of the hippocampus and parahippocampal gyrus are removed. The surgical procedure has been described in detail elsewhere.^{40,41,43} Between 1991 and 1999 (when the second group underwent surgery), SelAH became the main surgical procedure. Briefly, transcortical SelAH, a procedure that has been described in greater detail elsewhere,42,43 involves performing either a pterional craniotomy or a centered craniectomy with incision along the superior bank of the second temporal gyrus, and subpial extension of this line of entry down along the superior temporal sulcus, across the temporal white matter, and into the temporal horn of the lateral ventricle. Inside the ventricle, the hippocampus, amygdala, entorhinal cortex, and uncus are resected by endopial technique until the tectum, and the steps of the procedure are performed with neuronavigation. The evolution of the surgical procedure paralleled the advancements in neuroimaging techniques and the understanding of the epileptogenic basis of MTLE/HS.

Histopathological Study

Hippocampal tissue sufficient for histopathological diagnosis was available in all patients. The resected specimens were histopathologically examined with previously described techniques.³³ A standard neuropathological protocol was generally used for all epilepsy cases. The qualitative assessment of pattern of cell loss, gliosis, and HS in hippocampal subfields CA1, CA3, and in the dentate gyrus was applied.

Postoperative Evaluation

Follow-up examinations were conducted at 6 weeks, 6 months, and yearly thereafter through outpatient visits. All patients underwent MR imaging, scalp EEG, and neuropsychological evaluations during the follow-up period. Seizure outcome at the 1-year follow-up was based on the modified Engel classification system.⁷ For categorical comparisons, Engel classification was divided into favorable (Engel Classes I and II) and unfavorable (Engel Classes III and IV) seizure outcome.

Statistical Analysis

All data collected from each patient were organized in a database (Excel, Microsoft Corp.). Numeric variables were provided as the mean \pm SD. Preoperative group differences with respect to cognitive function and patient demographics, such as age at onset and seizure frequency, were evaluated using multivariate ANOVA to specify surgical approach (CAH vs SelAH) and laterality (right vs left) as group factors. A separate ANOVA was performed for each domain of cognitive function (IQ and verbal and nonverbal memory). Postoperative changes were assessed by repeated ANOVA with surgical approach (CAH vs SelAH) and laterality (left vs right) as between-group factors and cognitive domains as within-group factors. For categorical variables (seizure outcome or sex), the chi-square test was used. Changes within groups (preoperative vs postoperative) were assessed with paired ttests for paired samples. A p value < 0.05 was considered statistically significant. All statistical calculations were performed using commercially available software (SPSS version 14.0, SPSS, Inc.).

Results

Patient Characteristics

A summary of patients' clinical characteristics is provided in Table 1. The patient groups did not differ on sex (p = 0.13, chi-square test) and handedness (p = 0.18, chi-square test) with respect to side and type of surgery. Multivariate ANOVA revealed an interaction effect of "surgery X side" for mean age at epilepsy onset (F = 5.86, p = 0.016) and for duration of epilepsy (F = 4.2, p = 0.04). Patients in whom the surgery was performed on the left side were younger than those in whom it was performed on the right side (F = 7.79, p = 0.006). Thus, patients undergoing left CAH were younger at the onset



Fig. 1. Bar graph showing seizure outcome at the 1-year follow-up in patients who underwent SeIAH and CAH. No statistically significant difference was found between the groups with respect to side and type of surgery (p > 0.05, chi-square test). FO = Favorable outcome (Engel Classes I and II); UFO = unfavorable outcome (Engel Classes III and IV).

of epilepsy than those undergoing left SelAH, but the duration of epilepsy was longer in SelAH-treated patients regarding both sides. No difference was noted between the right- and left-sided surgery groups regarding preoperative mean seizure frequency (F = 0.51 and 0.47).

Seizure Outcome

Seizure outcome in each subclass of Engel classification at the 1-year follow-up is provided in Table 2, and the results according to side and type of surgery are provided in Fig. 1. Overall, 206 (80.5%) of the 256 patients were classified as having a favorable outcome. Ninety-nine (80.4%) of the 123 patients who underwent CAH and 107 (80.4%) who underwent SelAH were classified as having a favorable outcome. No significant association was detected between the surgical procedures and seizure outcome (p > 0.05, chi-square test).

Intelligence Outcome

Table 3 lists the IQ scores before and 1 year after surgery. The multivariate ANOVAs with type of surgery and laterality as intergroup factors revealed that there were no significant preoperative group differences with respect to FIQ (F = 2.0, p = 0.15), VIQ (F = 2.3, p = 0.12), and PIQ (F = 0.5, p = 0.45) before surgery. Regarding left-sided surgery, FIQ, VIQ, and PIQ all increased after CAH, but significant increases were seen in FIQ and PIQ (both p < 0.01, paired t-test). After SeIAH, FIQ and PIQ increased while VIQ decreased, but none of the differences showed significant changes (p > 0.05, paired t-test). In the rightsided resections, most of the IQ scores showed significant improvements after both types of surgery. In the CAH group significant postoperative increases were seen in all IQ groups (p < 0.001, paired t-test), but in the SeIAH

TABLE 2: Postoperative Engel outcome class at the 1-ye	ar
follow-up in patients with MTLE*	

	No. of Patients (%)						
		Rt Hen	nisphere	Lt Hen	Lt Hemisphere		
Engel Class	Total (256 patients)	CAH (63 patients)	SeIAH (61 patients)	CAH (60 patients)	SeIAH (72 patients)		
I							
a b c d	121 (47.3) 24 (9.4) 8 (3.1) 7 (2.7)	32 (50.8) 9 (14.3) 3 (4.8) 3 (4.8)	31 (50.8) 4 (6.6) 0 (0) 2 (3.3)	25 (41.7) 4 (6.7) 5 (8.3) 0 (0)	33 (45.8) 6 (8.3) 0 (0) 2 (2.8)		
11	× 7	()	. ,	()	× 7		
a b c d	12 (4.7) 27 (10.5) 0 (0) 7 (2.7)	0 (0) 9 (14.8) 0 (0) 0 (0)	2 (3.3) 9 (14.8) 0 (0) 3 (4.9)	6 (10.0) 1 (1.7) 0 (0) 2 (3.3)	4 (5.6) 9 (12.5) 0 (0) 2 (2.8)		
a b	29 (11.3) 0 (0)	3 (4.8) 0 (0)	4 (6.6) 0 (0)	10 (16.7) 0 (0)	12 (16.7) 0 (0)		
IV							
a b	18 (7.0) 3 (1.2)	4 (6.3) 0 (0)	6 (9.8) 0 (0)	5 (8.3) 2 (3.3)	3 (4.2) 1 (1.4)		
outcome							
FO UFO	206 (80.5) 50 (19.5)	56 (88.9) 7 (11.1)	51 (83.6) 10 (16.4)	43 (71.7) 17 (28.3)	56 (77.8) 16 (22.2)		

* FO = favorable outcome (Engel Classes I and II); UFO = unfavorable outcome (Engel Classes III and IV).

group significant improvements were demonstrated in FIQ (p = 0.02, paired t-test) and PIQ (p = 0.009, paired t-test) but not in VIQ. Figure 2 shows the changes (post-operative – preoperative value) within each group. A repeated measures of multivariate ANOVA with approach and laterality as intergroup factors indicated different results in postoperative changes. "Surgery X side" interactions reached significance regarding FIQ (F = 5.20, p = 0.06) and PIQ (F = 3.18, p = 0.04) scores, and losses were found to be greater after SelAH on both sides. No effect of "surgery X side" interactions was found with respect to VIQ (F = 2.23, p = 0.08), meaning that VIQ generally decreases after epilepsy surgery irrespective of side or type of approach.

Verbal Memory

The raw scores with respect to the domains of verbal memory are shown in Table 3. Preoperatively, the multivariate ANOVA showed that a "surgery X side" interaction approached a significant level for mean scores on the immediate (F = 4.8, p = 0.029) and delayed (F = 5.6, p = 0.018) LM recalls. Thus, the right CAH group tended to score better than the right SelAH group, but the left CAH group tended to score worse than left SelAH group in immediate LM recall. The right and left CAH groups scored better than their SelAH counterparts. Regarding the RAVLT, preoperatively a "surgery X side" interaction

		Rt Hem	isphere		Lt Hemisphere			
	CAH (63	3 patients)	SeIAH (61 patients)		CAH (60 patients)		SeIAH (72 patients)	
Variables	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop
WAIS-R								
FIQ	93.5 ± 15.9	98.3 ± 16.2	91.3 ± 11.6	92.5 ± 11.8	88.6 ± 12.8	93.4 ± 12.3	91.2 ± 13.7	91.8 ± 14.2
VIQ	93.1 ± 14.9	95.5 ± 14.8	91.2 ± 12.9	91.8 ± 12.4	87.6 ± 12.6	93.4 ± 12.3	91.3 ± 13.9	90.3 ± 15.2
PIQ	95.0 ± 19.2	101.5 ± 17.7	92.8 ± 11.1	95.7 ± 13.3	92.2 ± 14.9	98.2 ± 14.8	92.9 ± 15.2	94.9 ± 15.1
VLMT								
WMS-LM								
imm rec	11.1 ± 15.9	10.9 ± 16.6	8.7 ± 3.2	8.5 ± 3.0	6.8 ± 1.7	4.0 ± 2.8	7.4 ± 3.2	6.3 ± 3.1
del rec	9.2 ± 5.4	10.0 ± 5.7	6.6 ± 3.7	6.8 ± 4.1	7.7 ± 4.7	7.0 ± 4.6	5.2 ± 4.2	4.6 ± 3.4
RAVLT								
total score	35.1 ± 19.6	32.6 ± 18.4	47.0 ± 9.9	47.1 ± 9.6	42.4 ± 9.8	37.8 ± 9.9	44.6 ± 13.8	40.9 ± 12.0
imm rec	11.6 ± 3.6	11.3 ± 3.6	9.6 ± 3.3	9.3 ± 3.5	7.7 ± 3.2	7.3 ± 3.4	8.4 ± 3.4	7.4 ± 3.1
del rec	10.0 ± 3.5	10.3 ± 3.5	10.1 ± 3.1	10.1 ± 3.9	8.1 ± 4.0	6.6 ± 4.1	8.0 ± 3.7	6.8 ± 3.3
recognition	11.5 ± 3.0	10.5 ± 3.7	11.2 ± 4.0	11.5 ± 4.4	13.1 ± 2.6	13.4 ± 2.0	12.3 ± 3.0	11.7 ± 3.1
NVMT								
drawing								
imm rec	8.7 ± 2.7	7.9 ± 3.3	8.9 ± 4.1	8.4 ± 4.1	9.0 ± 2.2	9.5 ± 2.0	9.1 ± 2.7	9.2 ± 2.8
del rec	5.6 ± 3.3	5.2 ± 4.1	7.0 ± 3.9	6.8 ± 4.0	6.8 ± 3.1	7.5 ± 3.2	6.5 ± 3.5	7.1 ± 3.8
RCFT								
сору	25.0 ± 6.9	24.3 ± 6.3	24.6 ± 5.9	24.1 ± 7.9	26.9 ± 4.9	26.7 ± 5.4	24.1 ± 6.6	25.1 ± 5.1
del rec	10.5 ± 5.1	9.7 ± 5.7	11.3 ± 5.3	11.4 ± 6.4	13.7 ± 8.0	15.0 ± 5.9	11.6 ± 5.8	12.9 ± 6.7

TABLE 3: Cognitive test parameters before and 1 year after the 2 surgical approaches in patients with MTLE*

* Values are provided as raw data. Abbreviations: del rec = delayed recall; imm rec = immediate recall; NVMT = nonverbal memory tests; RCFT = Rey Complex Figure Test; VMLT = verbal learning and memory tasks.

showed significance on immediate (F = 12.6, p = 0.001) and delayed (F = 11.7, p = 0.001) recalls and word recognition (F = 6.37, p = 0.0013). Thus, the right CAH group had better scores than the right SelAH group regarding immediate recall and recognition, but on delayed recall the right SelAH group scored better than the right CAH group. For the left-sided resections, the CAH group tended to score better than the SelAH group regarding word recognition, but regarding immediate recall the CAH group scored worse than the SelAH group before surgery. Regarding postoperative verbal memory changes, different results were found with respect to immediate and delayed recall of prose passages. In the left-sided resections, both immediate and delayed recalls of LM decreased after either SelAH or CAH, but significant decline was noted in immediate LM recall in the SelAH group (p = 0.02, paired t-test) and in the CAH group (p < 0.01, paired ttest) with greater losses in the left CAH group (Fig. 3 left). In the right-sided resections, immediate recall decreased, but improvement was seen in delayed LM recall tests after both surgical approaches; however, paired t-tests did not show significant postoperative changes. Regarding RAVLTs, most of the domains decreased after both procedures on both sides, and greater losses were noted after left-sided resections (Fig. 3 right). Paired t-tests showed significant decrease in total score (p = 0.002), and immediate (p = 0.03) and delayed (p = 0.03) recalls and recognition (p = 0.03) after left SelAH. In the same way, left CAH caused a significant decrease in total score (p = 0.002) and delayed recall (p = 0.003). In the right-sided resections, the 2 surgical types lessened most of the domains, but none of the postoperative differences reached a significant level. Postoperatively, a repeated measures of multivariate ANOVA with approach and laterality as intergroup factors indicated significant "surgery X side" interactions only for immediate recall of LM (F = 5.4, p = 0.005), suggesting that the left-sided CAH has more negative effect on this cognitive function. A better preoperative score on immediate recall of LM was associated with a worse postoperative score after left CAH. Regarding RVALT, significant "surgery X side" interactions were found only for word recognition (F = 7.4, p = 0.007), and losses were greater after left SeIAH.

Nonverbal Memory

The raw scores in the domains of verbal memory are shown in Table 3. The multivariate ANOVAs with approach and laterality as intergroup factors revealed that there were no significant preoperative group differences with respect to immediate recall (F = 0.06, p = 0.80) and delayed recall (F = 0.34, p = 0.55) of simple geometric drawings. The subtests of the ROCF tests including copy (F = 2.14, p = 0.14) and delayed recall (F = 2.98, p = 0.08) also did not show any difference with respect to "surgery X side" interactions. Paired t-tests showed that immediate



Fig. 2. Bar graph showing difference in scores in intelligence (postoperative – preoperative) depending on the side and type of surgery. Positive and negative values show improvement and impairment, respectively. *p < 0.05, paired t-test.

(p < 0.01) and delayed (p = 0.03) recall of simple geometric drawings significantly improved after left-sided surgery, preferentially after left CAH. However, on the right-sided resections, both surgical approaches showed impairments on both tests; this was more frequent after CAH. However, the impairments were not statistically different from preoperative measures (Fig. 4 *left*). The ROCF tests showed improvement after left-sided surgery with significant improvement in copy (p = 0.04, paired t-test) and delayed recall (p = 0.02, paired t-test) after left SelAHs. On the right side, greater impairment was seen after CAH. We noted a little improvement in delayed recall after SelAH, but none of the postoperative changes regarding right-sided resections showed significant differences (Fig. 4 *right*). Postoperatively, a repeated measures of multivariate ANOVA with approach and laterality as intergroup factors indicated no significant "surgery X side" interactions for immediate recall of simple geometric drawings (F = 1.86, p = 0.13) and copy (F = 0.65, p = 0.58) of the ROCF test. However, a main effect of type and side of surgery interaction was found for delayed recall of the ROCF test (F = 6.15, p = 0.001) and was preferentially worse after right-sided surgery (right CAH).

Epilepsy Variables and Cognitive Performance

Pearson correlation analysis demonstrated different correlation patterns for those who underwent left- or rightsided surgery. For left-sided cases, age at surgery was negatively correlated with delayed LM recall (p = 0.001) and with the word recognition domain of the RAVLT in cases of CAH, suggesting that later surgery can lead to poor verbal memory. Duration of epilepsy was also negatively correlated with delayed recall of LM (p = 0.007) in CAH cases; the shorter the duration, the better the delayed verbal memory. Furthermore, preoperative seizure frequency in the CAH cases showed a negative correlation with verbal material (recognition) (p = 0.004); a greater seizure frequency predicted poorer verbal memory. Poor postoperative seizure control in CAH cases was associated with poorer recall of some verbal (delayed recall of LM; p =(0.00001) and nonverbal (copy of ROCF test; p = 0.00001) materials, showing that ongoing seizure activity was disrupting stored information. None of the variables showed any correlation with the cognitive functions tested here in SelAH cases. For right-sided cases, seizure duration negatively correlated with copy of the ROCF tests (p =0.001) in patients who underwent CAH; a longer seizure



Fig. 3. Bar graph showing difference in scores (postoperative – preoperative) in verbal memory using WMS-LM depending on the side and type of surgery. Immediate/delayed recalls of 15 words (*left*) and domains of the RAVLT (*right*) are shown. Positive and negative values show improvement and impairment, respectively. Del. = delayed; Imm. = immediate. *p < 0.05, paired t-test.



Fig. 4. Bar graph showing difference in scores (postoperative – preoperative) in nonverbal memory using simple geometric drawings (*left*) and ROCF test (*right*) depending on the side and type of surgery. Positive and negative values show improvement and impairment, respectively. *p < 0.05, paired t-test.

duration was associated with poorer results for at least some components of nonverbal memory. Age at surgery and age at onset did not show any correlation with any of the tests included in this study in either CAH or SelAH cases. Seizure freedom was correlated with better recall of verbal memory (delayed recall of LM) (p = 0.005) in both CAH and SelAH.

Surgical Complications

No patient died in this series. However, 2 patients (0.7%) experienced surgical complications. One patient had a subgaleal fluid collection, which did not require any intervention, and the other had osteomyelitis, which required bone flap replacement. The postoperative period was uneventful, and the patient was discharged without any other complication.

Discussion

Main Findings

This study documents 1-year postoperative memory outcomes and general intelligence changes in 256 adult patients who underwent either CAH or SelAH for MTLE. The main findings that can be drawn from this study are as follows: 1) Seizure outcome is not significantly different between the 2 surgical approaches at the 1-year follow-up. 2) The side of surgery has no effect on seizure outcome. 3) General intelligence increases after epilepsy surgery, but VIQ is particularly affected by left SelAH. 4) Significant losses are generally seen in verbal learning and recognition after left-sided surgery. 5) Left-sided surgery irrespective of type showed improvements in nonverbal memory. 6) Slight decline in figural learning and memory was preferentially observed after right CAH. 7) Late surgery and/or longer duration of epilepsy are generally associated with poorer memory. 8) Better seizure outcome, especially seizure freedom, leads to improvement in memory functions. Since the seminal works of Scoville and Milner⁵⁰ and Penfield and Milner⁴⁷ who-in their studies of patients with amnesia-showed that the mesial temporal structures play an important role in human memory, there has been much discussion regarding which resection in MTLE would be appropriate to prevent cognitive disturbances, which otherwise can overshadow successful surgery. Although there is no common notion on the surgical strategy, it is generally accepted that leftsided (dominant) temporal resections produce deficits in verbal learning and recall, but right-sided (nondominant) resections cause deficits in visuospatial memory. For the purpose of our study (CAH vs SelAH), we will focus on comparative studies assessing the effect of side and type of surgery on memory outcome.

Comparative Studies

As far as we are aware, there have been at least 20 comparative studies in the English-language literature, and Table 4 summarizes the main findings. Several authors have reported better neuropsychological outcome for SelAH,^{13,16,19–21,35,44,45,55} but others have claimed that both CAH and SelAH produce similar deficits in cognitive functioning.^{11,12,17,26,27,52,63} In 1982, Wieser and Yaşargil⁶² found verbal memory deficits after left CAH but not after left SelAH and impairment in visual learning after right CAH but not after right SelAH. In 1992, using more global memory (the Rivermead Behavioral Memory Test) and Rey figure tests and Everyday Memory Questionnaire,12 Goldstein and Polkey11 did not show differences with respect to memory 15 months after surgery. They underlined that there was no evidence that SelAH results in a lesser degree of everyday memory impairment than CAH. A year later, Wolf et al.⁶³ showed no difference in cognitive outcome between the groups defined by the extent of either left mesial or left lateral cortical resections,

	No. of Patients			
Authors & Year	CAH	SelAH	FU Duration (mos)	Neuropsychology
Wieser & Yaşargil, 1982	5	6	21	SeIAH: less impairment
Goldstein & Polkey, 199211	25	21	15	no difference
Goldstein & Polkey, 199212	58	15	6	SeIAH: less impairment
Goldstein & Polkey, 1993	19	23	<6	SeIAH: short-term beneficial effect on memory
Wolf et al., 1993	30	17	6	no difference
Renowden et al., 1995	50	17	24	SeIAH: better for VIQ & nonverbal memory
Helmstaedter et al., 1996	22	21	3	SeIAH: better for immediate recall
Jones-Gotman et al., 1997	23	25	18	no difference in seizure-free patients
Helmstaedter et al., 1997	21	15	12	SeIAH: better for nonverbal memory
Pauli et al., 1999	16	26	NA	SeIAH: better for verbal memory
Hadar et al., 2001	14	14	NA	SeIAH: better for recall
Clusmann et al., 2002	83	126	38	SeIAH: better for verbal memory
Lacruz et al., 2004	91	15	11	no difference
Clusmann et al., 2004	35	54	12	SeIAH: less impairment in children
Hader et al., 2005	20	16	NA	no difference
Paglioli et al., 2006	45	41	36	SeIAH: better for verbal memory
Morino et al., 2006	17	32	12	SeIAH: better for memory function
Tanriverdi & Olivier, 2007	36	36	12	SeIAH: less decline for verbal memory
Helmstaedter et al., 2008	35	62	12	SeIAH: better for rt-sided resections for nonverbal memory
Shin et al., 2009	14	23	12	no difference
present study	123	133	12	SeIAH: less decline for verbal memory & better for rt-sided resections for nonverbal memory

TABLE 4: Studies comparing CAH with SeIAH for neuropsychological variables*

* FU = follow-up; NA = not available.

and that the risk of cognitive impairment was dependent more on age at seizure onset in patients with MTLE/HS. They stated that mesial or lateral structures ipsilateral to seizure focus minimally contribute to memory function as previously suggested.^{28,34,46}

A previously published study from our center compared seizure-free cases from 3 different centers after corticectomy (Dublin), SelAH (Zurich), and CAH (MNI) and found similar deficits in learning and retention of words and designs.²⁶ The patients in Dublin with left lateral temporal resection showed impairment with respect to the control individuals on every trial of the word list, but those who underwent right resections did not show deficits on the same test. For the design list, both left and right patient groups were significantly impaired compared with the controls. In the MNI study, a significant deficit was found in the left CAH group with respect to controls on every trial of the word list, but the right CAH group was not significantly impaired. For the design list, both the left and right CAH groups showed significant deficits in delayed recall compared with the controls. And finally the patients in the Zurich study showed a significant difference in word list performance for the left SelAH group with respect to controls in all trials, but the right CAH group was not significantly impaired. For the design list, the right SelAH group was significantly different from normal on every trial, while the left SelAH group was impaired. The authors concluded that retention of words was clearly impaired in every group of patients with left-sided

excision, but not among patient groups with right-sided excision; in contrast, retention of designs was not different among the various patient groups.²⁶

Some recent studies also confirmed findings from the aforementioned studies that CAH or SelAH can produce similar neuropsychological consequences.^{17,27,31} In contrast, there have been a considerable number of studies showing that type and side of surgery produce different cognitive deficits. Using traditional memory tests, Goldstein and Polkey¹³ showed that left-sided surgery caused clear deterioration in verbal memory after both CAH and SelAH, but to a lesser extent in SelAH, and that right CAH produced more deterioration than right SelAH on nonverbal tests. According to the authors, SelAH produced a short-term beneficial effect on memory.¹³ Furthermore, they showed that poor postoperative seizure control and later surgery were associated with poor postoperative verbal and/or nonverbal memory outcome.¹³ Renowden et al.⁴⁹ found that patients who underwent left SelAH (transcortical or transsylvian) showed significant improvement in VIQ and nonverbal memory over those who underwent left CAH. Both surgeries resulted in a decline in verbal memory, suggesting that both left mesial and lateral temporal cortex contribute to verbal memory. In 59 patients with left MTLE and left lesional epilepsy, Helmstaedter et al.¹⁹ reported that verbal memory did not change after cortical lesionectomy. In contrast, CAH and SelAH led to a significant deterioration in verbal memory, especially in recognition and free recall. However, different from SelAH and cortical resections, CAH led to a significant loss in total immediate recall 3 months after surgery. In another study, the Bonn group²⁰ showed that patients who underwent left CAH and SelAH had significantly deteriorated delayed recall and recognition when compared with those who underwent corticectomy. Patients who underwent CAH showed significant deterioration in total immediate recall when compared with those who underwent corticectomy and SelAH. Furthermore, a longer duration of epilepsy was found to be associated with poorer verbal memory. Thus, these results indicate that not only lateral temporal cortex but also mesial structures contribute to immediate recall and recognition. Pauli et al.45 found a significant loss in verbal memory in the left-sided CAH, and the efficiency of verbal retention was also markedly impaired after CAH compared with SelAH. Hadar et al.¹⁶ found that recall of the RAVLT was significantly better in the dominant hemisphere after SelAH and there was no advantage of a more limited resection in Boston naming.

It has been reported that postoperative neuropsychological performance is highly dependent on the presurgical findings. Patients with good verbal performance and a left-sided seizure focus preoperatively tended to exhibit deterioration after surgery; the rate of deterioration was significantly dependent on the resection type, and SelAH was found to be better than CAH on the left side regarding verbal memory in adults^{5,16} and children.⁴ Paglioli et al.44 showed that left-sided SelAH caused significant improvement in verbal memory, but the same effect was not seen after right-sided resections. They stated that selective resection, especially transcortical SelAH, should be the choice of approach in patients with left MTLE. A recent paper by Morino et al.35 showed no significant difference between the 2 surgical approaches with respect to IQ. Left-sided CAH and SelAH caused decline in VIQ and PIQ, respectively. They found that CAH and SelAH produced verbal and nonverbal memory decline after left- and right-sided resections, respectively, and memory function overall was better preserved in patients undergoing SelAH. Recently, we reported that verbal memory decreased after left-sided resection in CAH and SelAH, but the decline was much more pronounced in the left-sided SelAH group. On the other hand, the postoperative memory function was better preserved in the SelAH group compared with the CAH group in patients with MTLE undergoing right-sided resections.⁵⁷ In a recent prospective study comparing material-specific memory outcome in patients with MTLE after SelAH, CAH, and temporal pole resection with AH, Helmstaedter et al.²¹ demonstrated that verbal memory and figural memory losses were evident after left- and right-sided resections. Moreover, verbal memory after left-sided resections was significantly improved after temporal pole resection with AH, whereas the same was found to be true for the outcome in figural memory after right-sided SelAH. Nevertheless, as can be seen from the results of the studies discussed so far, SelAH appears to produce better memory outcome, although this is not a consistent finding.

Interpretation of the Present Study

Our results indicate that surgery irrespective of type

leads to improvement in general intelligence. The CAH approach showed improvement in VIQ, PIQ, and FIQ irrespective of side, and significant improvements were seen especially in PIQ and FIQ. After SelAH, most of the IO scores also improved. However, VIO decreased after left-sided SelAH, but the decline was not significant. Our results are consistent with the majority of previously published series,^{13,29,30,55} and findings including ours supported the common notion that epilepsy surgery results in very little improvement in overall intellectual functions.^{18,25,28} In addition, our results showed that changes in VIQ and PIO scores do not always permit diagnostic indicators of left and right hemisphere dysfunction. There was no difference between the 2 surgical procedures in terms of seizure control 1 year after surgery, which is in line with previous comparative studies.^{1,5,15,56} If there are no differences in seizure outcome between CAH and SelAH, one can assume that differences in cognitive functions mainly come from the resected lateral temporal neocortex. Theoretically, patients undergoing CAH can show deficits in both short- and long-term memory function.

The present study provides clear evidence of different effects of left and right temporal resections on verbal and nonverbal memory functions. For verbal memory, both left- and right-sided surgeries irrespective of type resulted in deterioration in immediate LM recall,³⁷ but significant decrease was seen after left-sided CAH. For the delayed LM recall, both approaches on the left side produced deterioration, whereas right-sided surgery (both SelAH and CAH) resulted in a mild improvement. The domains of RAVLT (total learning, immediate/delayed recall, and recognition) decreased significantly after leftsided SelAH. Furthermore, left-sided CAH also resulted in significant deterioration in total learning score and delayed recall. Right-sided surgery irrespective of type produced a mild degree of impairment of RAVLT, but the changes on the right side were not significant. Our results clearly support the assumed effects of different resections on different aspects of verbal memory,13,19-21,25,26,28,44,55 namely, that temporomesial structures mainly appear to be involved in long-term consolidation and retrieval processes. In contrast, verbal short-term memory or working memory depends on interaction of temporomesial and -lateral structures.⁶³ Regarding nonverbal memory, our results support the converging evidence in that nonverbal memory losses became evident particularly after rightsided surgery and left-sided surgery produced improve-ment in nonverbal memory.^{9,10,13,14,21,27,30,34,35,44,45,48,51,55}

For simple geometric drawings, both immediate and delayed recall improved after left-sided surgery irrespective of type, and significant improvements were seen after left CAH. However, both tests showed impairments in immediate and delayed recall after right CAH or SelAH, but improvements were more frequent after right-sided CAH. Left-sided surgery improved the domains (copy and delayed recall) of the ROCF tests, and significant improvement was seen after SelAH. However, right-sided CAH produced more deterioration than the SelAH, but the differences were not significant. Postoperatively only a significant "surgery X side" interaction was seen in delayed recall of ROCF tests, suggesting more deterioration after

right-sided CAH and superiority of SelAH over CAH on this measure. Our findings support the assumption that the lateral temporal neocortex is of particular importance for nonverbal memory. Consistent with previously published series,^{13,63} in the left-sided CAH group, older age at surgery and duration of epilepsy showed strong negative correlation with delayed recall of LM. Recognition memory showed negative correlation with older age at surgery and preoperative seizure frequency. As reported earlier,^{20,25} delayed recall requires retrieval from long-term encoded material and is more related to mesiolimbic structures. However, recognition is mainly a decision-making and matching process on the basis of encoded material and is less an active retrieval process.²⁰ Thus, our results suggest that delayed recall of LM and memory recognition depend more on the synergistic activity between the mesiolimbic and lateral temporal neocortex.

Poor seizure outcome in our study showed a strong correlation with poor verbal (delayed recall of LM) and nonverbal (copy of ROCF tests) memory. Overall, correlation analysis supports early surgery in patients with MTLE. On the right side, seizure duration negatively correlated with nonverbal memory (copy of ROCF tests) in the CAH group. Poor seizure control was correlated with delayed recall of LM in both CAH and SelAH groups.

The SelAH technique was originally developed in an attempt to avoid resection of unaffected brain tissue and thus to minimize negative cognitive consequences. There are several SelAH surgical techniques with their own advantages and disadvantages. The technique of SelAH, which was transcortical, was first proposed by Niemeyer³⁶ and modified and popularized by Olivier.^{42,43} Transsylvian SelAH was proposed by Yaşargil et al.,64 and recently Hori et al.22 suggested subtemporal SelAH to decrease cognitive impairments. One possible explanation for verbal memory decline after either transcortical or transsylvian SelAH could be due to the resection of the basolateral nucleus of the amygdala, which is known to enhance memory consolidation through the release of glucocorticoids,³⁸ or of entorhinal cortex.⁴⁴ Recently, Helmstaedter et al.²¹ have suggested that the unfavorable results of a verbal memory decline after a left transsylvian SelAH may be due to collateral (cortical) damage to temporal and frontal lobes and interruption of the temporal stem including the uncinate fasciculus, which is a major functional tract connecting the temporal and frontal lobes and also plays an important role in encoding, memory formation, and retrieval processes.³⁹ However, transcortical SelAH generally spares a portion of the temporal stem. Thus memory decline in our sample cannot be explained depending solely on these assumptions.²⁵ Using PET, Dupont et al.⁶ showed significant reduction in the metabolism of the temporal pole ipsilateral to transsylvian SelAH. This could explain the decline in memory that was previously associated with the temporal neocortex. In the same study, the authors noticed that there was a postoperative increase of normalized metabolic activity in the hippocampus contralateral to the surgery and in both orbitofrontal cortices. These findings suggested that elimination of or decreasing seizures may lead to improvement in the contralateral mesiolimbic and orbitofrontal regions, which could explain the improvement in nonverbal memory functions after left-sided surgery in the present study.^{9,21} Hori et al.²⁴ and Takaya and coworkers⁵³ reported preservation or improved cognitive functions after subtemporal SelAH, and the authors attributed this finding to the preservation of temporal structures. Whatever the type of selective approach, removing the mesiolimbic structures is not free of disruption of various temporal regions, which inevitably produces cognitive decline depending on the side of surgery.

Study Limitations

The main limitation of the current study is its retrospective and contemporaneous nature, given that the diagnoses and neuropsychological variables were obtained from the information registered in the charts, which could have introduced some collection bias. Therefore, it would be very useful if we could compare the findings regarding the precise extension of the mesial limbic or lateral cortex resection, which may have a significant effect on the patient's memory outcome. Finally we want to underline that our findings are not novel and in fact reproduce what has been published so far.

Conclusions

Despite advanced diagnostic techniques in MTLE, we are still far from an optimal surgical approach for better cognitive outcome. The present study provides evidence that type and side of surgery are important with respect to verbal and nonverbal memory outcomes. An SelAH is not advantageous over a CAH. Thus, we suggest that the optimal type of surgical approach should be decided on a case-by-case basis.

Disclosure

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